



Europäisches Patentamt
European Patent Office
Office européen des brevets



Publication number: **0 296 321 B1**

EUROPEAN PATENT SPECIFICATION

- (43) Date of publication of patent specification: **23.09.92** (51) Int. Cl.⁵: **C07F 15/00**
(21) Application number: **88105673.3**
(22) Date of filing: **09.04.88**

(54) **Synthesis of cisplatinum analogs.**

- (30) Priority: **23.06.87 US 65441**
(43) Date of publication of application:
28.12.88 Bulletin 88/52
(45) Publication of the grant of the patent:
23.09.92 Bulletin 92/39
(84) Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI NL SE
(56) References cited:

CHEMICAL, vol. 102, no. 3, 21st January 1985,
page 712, column 2, abstract no. 24808v,
Columbus, Ohio, US; S. LANZA, et al.:
"Dissociative substitution in four-coordinate
planar platinum (II) complexes. Kinetics of
sulfoxide exchange and displacement by
bidentate ligands in the reactions of cis-
diarylbis(dimethyl sulfoxide)platinum(II) in
chloroform and benzene, & INORG. CHEM.
1984, 23(26), 4428-4433

- (73) Proprietor: **AMERICAN CYANAMID COMPANY**
1937 West Main Street P.O. Box 60
Stamford Connecticut 06904-0060(US)
(72) Inventor: **Bitha, Panayota**
287 Treetop Circle
Nanuet New York 10954(US)
Inventor: **Hiavka, Joseph John**
Tower Hill Road
Tuxedo Park New York 10987(US)
Inventor: **Lin, Yang-I**
35 Constitution Drive
Tappan New York 10983(US)
(74) Representative: **Wächtershäuser, Günter, Dr.**
Tal 29
W-8000 München 2(DE)

Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid (Art. 99(1) European patent convention).

CHEMICAL ABSTRACTS; vol. 98, no. 22, 30th May 1983, page 428, columns 1-2, abstract no. 186358z, Columbus, Ohio, US; L.E. ERICKSON et al.: "Kinetics and mechanisms of ligand exchange, substitution, and isomerization of Me₂SO-amino acid complexes of platinum(II): evidence for a pseudorotation mechanism", INORG. CHEM. 1983, 22(10), 1461-1467

CHEMICAL ABSTRACTS, vol. 94, no. 8, 15th-29th June 1981, page 403, columns 1-2, abstract no. 198169u, Columbus, Ohio, US; M. BONIVENTO et al.: "Kinetics of displacement of dimethyl sulfoxide from cis-dichlorobis(dimethyl sulfoxide)platinum(II) by amines in dimethoxyethane", & INORG. CHEM. 1981, 20(5), 1493-1496

JOURNAL OF ORGANOMETALLIC CHEMISTRY, vol. 170, no. 1, 24th April 1979, pages C18-C20, Lausanne, CH; C. EABORN et al.: "Alkyl- and aryl-platinum(II) complexes from K₂(PtCl₄) and tetraorganotin compounds in dimethylsulphoxide. Preparation and reactions of complexes (PtR₂(DMSO)₂) and (PtR(C)(DMSO)₂)

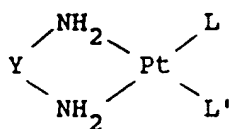
JOURNAL OF THE CHEMICAL SOCIETY, DALTON TRANSACTIONS, 1986, pages 1101-1105; G. ANNIBALE et al.: "Kinetics and mechanism of the reaction between dimethyl sulfoxide and dichloro(pyridine-2-carboxylato)platinum(II) anion and the cis-trans isomerization of the products. X-Ray crystal structure of trans-(0,S)-chloro(dimethyl)sulphoxide(pyridine-2-carboxylato)platinum(II)"

CHEMICAL ABSTRACTS, vol. 99, no. 20, 14th November 1983, page 650, column 1, abstract no. 168415g, Columbus, Ohio, US; R. I. RUDYI et al.: "Reactions of complexes of platinum(III) with dimethyl sulfoxide", & IZV. AKAD. ANUK SSSR, SER. KHIM. 1983, (8), 1866-1871

South African Patent 87/0713 and 87/9714 cited in the application

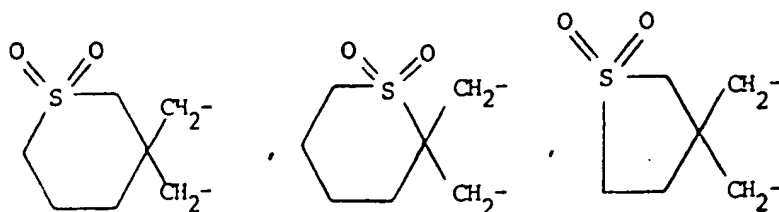
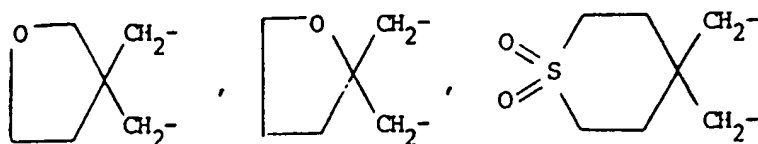
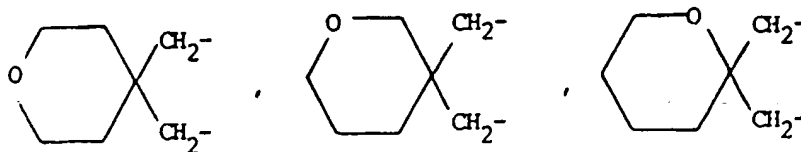
Description

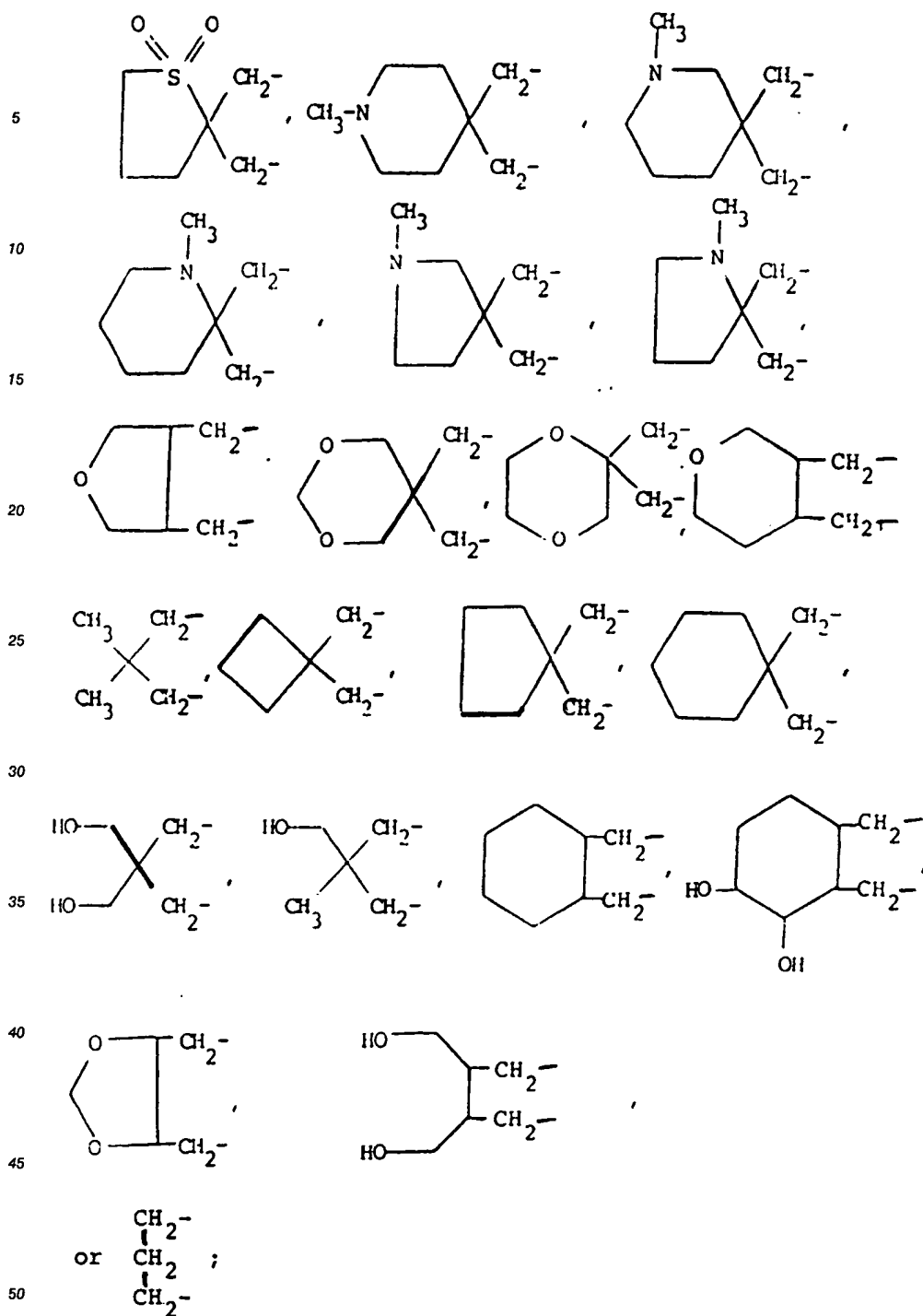
This invention is concerned with a process for producing compounds of The formula I:



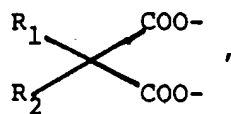
Formula I

wherein Y is selected from the group consisting of





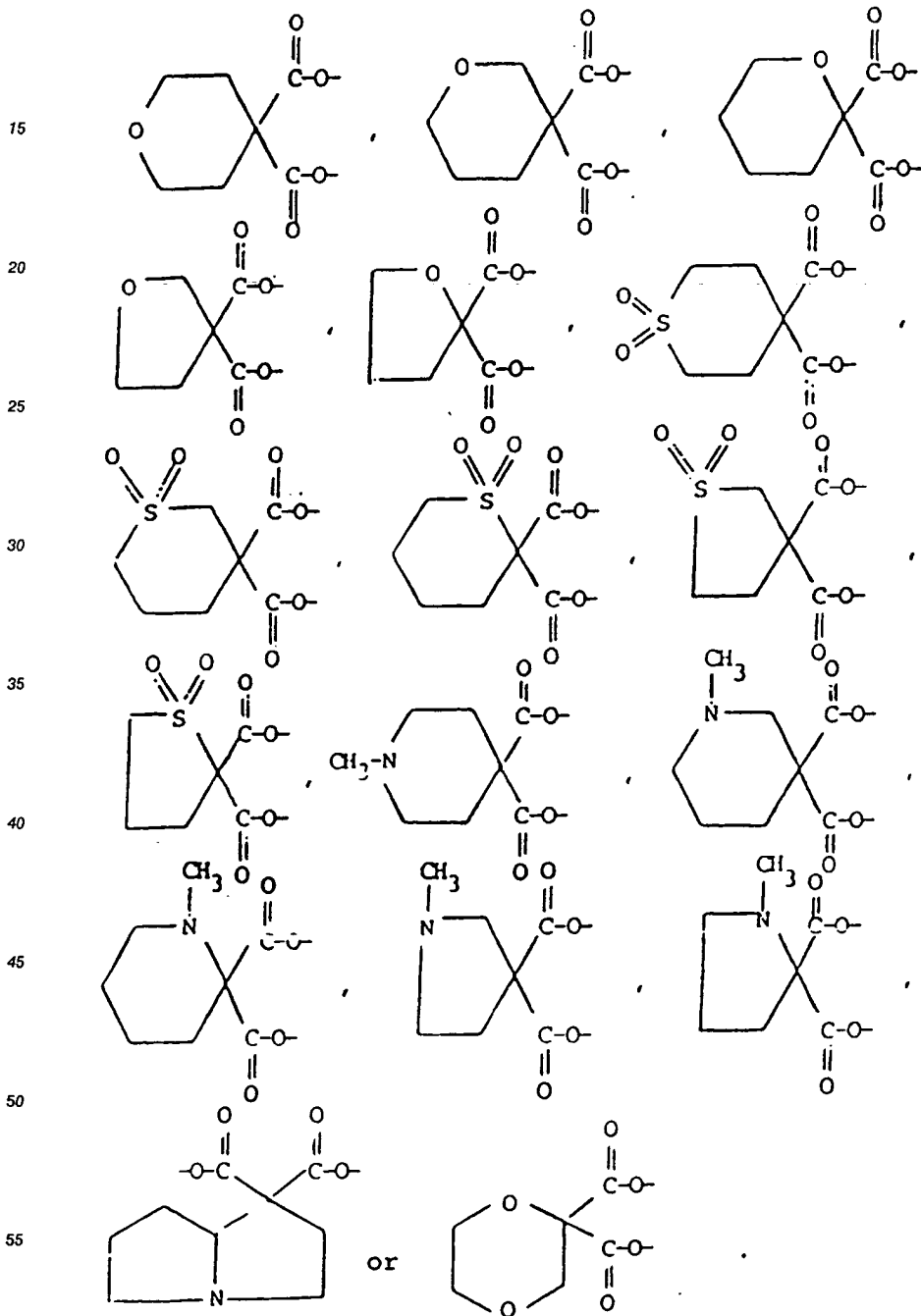
and L and L' are monobasic carboxylates consisting of acetate, hydroxyacetate or propionate, or L and L' taken together are a dibasic carboxylate consisting of



5

wherein R_1 and R_2 are hydrogen or lower alkyl (C_1 - C_5) or R_1 and R_2 taken together is $(CH_2)_n$, wherein n is 2 to 5,

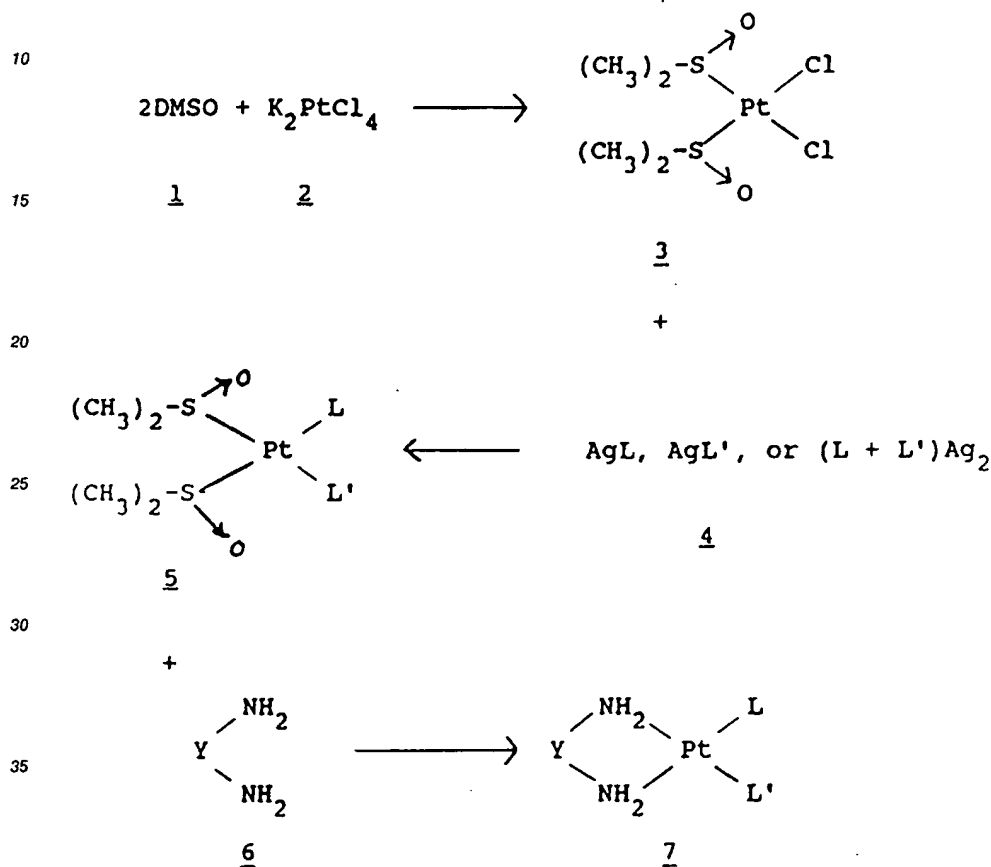
10



The compounds described in Formula I are highly active antitumor agents. Their activity as such has been disclosed in the following South African patents 87/0714, issued September 30, 1987 and 87/0713, issued January 1, 87.

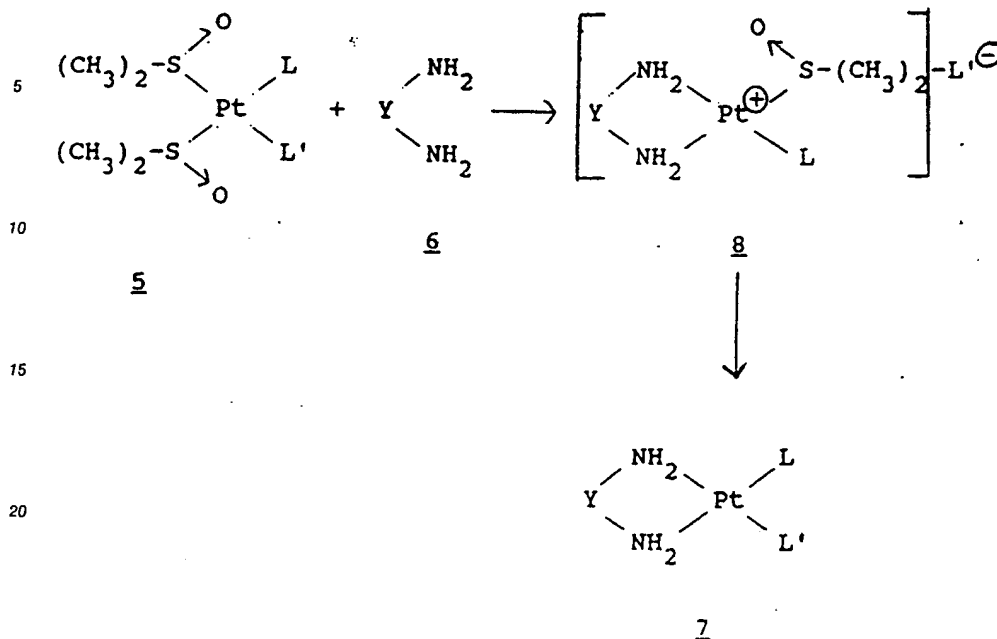
The process, with which the current invention is concerned, is described below by flowchart and text.

Flowchart A



40 In accordance with flowchart A, dimethyl sulfoxide 1 is reacted with potassium tetrachloroplatinate 2 in aqueous solution to produce sulfinyl bismethane, compound with platinum dichloride (2:1) 3. Compound 3 is then reacted with a mono- or dicarboxylic acid silver salt (L, L' or L + L') 4 in aqueous solution, protected from light, giving carboxylic acid-bis[sulfinylbis[methane]-S]platinum derivative 5. Compound 5 is then

45 reacted with an amine 6 in a hot aqueous solution giving the final, pharmacologically active product 7 - (Formula I).

Flowchart B

In accordance with Flowchart B, a carboxylic acid-bis[sulfinylbis[methane]-S]platinum derivative 5 is reacted with an amine 6 in a warm aqueous solution, giving an amine, carboxylic acid [sulfinylbis[methane]-S]platinum derivative 8, which on heating in aqueous solution gives the biologically active derivative 7.

The intermediates 5 and 8 are unknown in the art and since they are integral in the preparation of pharmaceutically useful products, they will be claimed as new compounds as a part of this invention.

The invention will be described further in conjunction with the following specific examples.

Example 1[1,1-Cyclobutanedicarboxylato(2-)-O,O']bis[sulfinylbis[methane]-S]platinum

To a solution of 41.5 g of potassium tetrachloroplatinate in 330 ml of water was added 21.3 ml of dimethyl sulfoxide. The mixture was allowed to stand 12 hours, then the solid was collected, washed with water, ethanol and ether, giving 38.0 g of sulfinyl bismethane, compound with platinum chloride (2:1), mp 222° C (dec.).

A mixture of 12.66 g of the above compound, 10.74 g of the disilver salt of 1,1-cyclobutanedicarboxylic acid and 900 ml of water was stirred in the dark for 22 hours and then filtered. The filtrate was concentrated to 40 ml and the precipitate collected, giving 12.4 g of [1,1-cyclobutanedicarboxylato(2-)-O,O']bis[sulfinylbis[methane]-S]platinum, mp 208° C (dec.).

This compound (494 mg) in a hot solution of 12 ml of water, was reacted with a hot solution of 114 mg of trans-(-)-1,2-cyclohexanediamine in 3 ml of water. The mixture was kept at 100° C for 6 hours, then cooled, giving 360 mg of biologically active trans-(-)-1,2-cyclohexanediamine, compound with [1,1-cyclobutanedicarboxylato(2-)-O,O']platinum (1:1).

Example 2Preparation of [1,1-Cyclobutanedicarboxylato(2-)-O,O'](1,3-dioxane-5,5-dimethanamine-N,N')-platinum

A suspension of 26.2 g of 2,2-bis(bromomethyl)-1,3-propanediol, 50 ml of concentrated hydrochloric acid and 50 ml of 38% formaldehyde was stirred in a 50° C oil bath overnight, then cooled to room temperature and filtered. The filtrate was extracted with three 100 ml portions of ether. The ether extracts

were combined, washed with water, dried and evaporated to an oil. A small amount of solid which formed was removed by filtration and washing with ether. The combined filtrate and wash was evaporated under reduced pressure, giving 26.9 g of 5,5-bis(bromomethyl)-1,3-dioxane as a clear oil.

A suspension of 2.69 g of 5,5-bis(bromomethyl)-1,3-dioxane, 3.8 g of sodium azide and 50 ml of dimethylformamide was heated at 130 °C in an oil bath overnight, then cooled and filtered. The filtrate was evaporated to an oily suspension which was diluted with 30 ml of water. The oily phase was extracted with three 25 ml portions of ether. The ether extracts were combined, dried and evaporated, giving 1.95 g of 5,5-bis(azidomethyl)-1,3-dioxane.

A mixture of 1.95 g of 5,5-bis(azidomethyl)-1,3-dioxane, 0.5 g of 10% palladium on calcium carbonate and 40 ml of ethanol was reduced for 2 hours and then filtered. The filtrate was evaporated, giving 1.41 g of 1,3-dioxane-5,5-dimethanamine as an oil.

A 1.97 g portion of [1,1-cyclobutanedicarboxylato(2-)-O,O']bis[sulfinylbis(methane)-S]platinum was dissolved in 48 ml of hot (100 °C) water. To this was added a solution of 585 mg of 1,3-dioxane-5,5-dimethanamine in 12 ml of water. The mixture was stirred at 100 °C for 6 hours and then evaporated to dryness. The residue was dissolved in 2 ml of hot water and filtered. The filtrate was cooled, then refrigerated for 2 hours and the solid collected, giving 606 mg of biologically active [1,1-cyclobutanedicarboxylato(2-)-O,O']-(1,3-dioxane-5,5-dimethanamine-N,N')platinum.

Example 3

Preparation of [1,1-Cyclobutanedicarboxylato(2-)-O',O']-(tetrahydro-4H-pyran-4,4-dimethanamine-N,N')platinum

A mixture of 28.6 g of dichloroethyl ether, 13.2 g of malononitrile, 55.28 g of potassium carbonate and 800 ml of acetonitrile was refluxed on a steam bath for 24 hours, then filtered while hot. The filtrate was evaporated and the residue crystallized, with charcoal treatment, from 100 ml of ethanol, giving 9.5 g of tetrahydro-4H-pyran-4,4-dicarbonitrile as colorless plates, mp 110-112 °C.

A 180 ml portion of 1N borane in tetrahydrofuran was added rapidly, dropwise to a solution of 8.18 g of tetrahydro-4H-pyran-4,4-dicarbonitrile in 150 ml of tetrahydrofuran. This mixture was warmed, then cooled to room temperature in an ice bath and then stirred for 64 hours at room temperature. A 100 ml portion of ethanol was added dropwise, then the mixture was stirred 4 hours and evaporated to dryness. The residue was taken up in 100 ml of water, acidified with 50 ml of 6N hydrochloric acid and extracted three times with ether. The remaining aqueous layer was evaporated to dryness. The residue was boiled in 300 ml of methanol and filtered while hot. The filtrate was treated with 200 ml of ether and cooled. The resulting solid was collected, washed with ether and dried, giving 8.31 g of tetrahydro-4H-pyran-4,4-dimethanamine, dihydrochloride.

An ion exchange resin (Dowex, 1-X4) was slurried in 10N sodium hydroxide and then packed into a 3/4 inch column. The column was washed with water until the pH was neutral. An aqueous solution of 2.17 g of tetrahydro-4H-pyran-4,4-dimethanamine, dihydrochloride was added to the column at a slow flow rate. The column cut containing the free base was evaporated, giving 1.48 g of tetrahydro-4H-pyran-4,4-dimethanamine as a colorless oil.

A 4.9 g portion of [1,1-cyclobutanedicarboxylato(2-)-O,O']bis[sulfinylbis(methane)-S]platinum was dissolved in 120 ml of water at 100 °C. A solution of 1.4 g of tetrahydro-4H-pyran-4,4-dimethanamine in 30 ml of water was added and the mixture was heated at 100 °C for 6 hours. The mixture was filtered and the filtrate evaporated to dryness. The residue was slurried in 30 ml of water, heated to 95 °C and filtered. The filtrate was concentrated to about 10 ml and the resulting solid collected, washed with water and dried, giving 1.34 g of biologically active [1,1-cyclobutanedicarboxylato(2-)-O',O']-(tetrahydro-4H-pyran-4,4-dimethanamine-N,N')platinum.

Example 4

Preparation of [2,2-Bis(aminomethyl)-1,3-propanediol-N,N']-[1,1-cyclobutanedicarboxylato(2-)-O',O']-platinum

To a solution of 1.0 g of [1,1-cyclobutanedicarboxylato(2-)-O,O']bis[sulfinylbis(methane)-S]platinum in 25 ml of water at 100 °C was added a solution of 272 mg of 2,2-bis(aminomethyl)-1,3-propanediol in 5 ml of water. The mixture was heated at 100 °C for 6 hours and then filtered. The filtrate was evaporated to about 3 ml and the resulting solid collected, giving 100 mg of biologically active [2,2-bis(aminomethyl)-1,3-

propanediol-N,N'][1,1-cyclobutanedicarboxylato(2-)-O',O']platinum.

Example 5

5 Preparation of 2,2-Dimethyl-1,3-propanediamine, compound with [1,1-cyclobutanedicarboxylato(2-)-O',O']-platinum

To a warm solution of 1.24 g of [1,1-cyclobutanedicarboxylato(2-)-O',O']bis[sulfinylbis(methane)-S]-platinum in 60 ml of water was added 0.26 g of 2,2-dimethyl-1,3-propanediamine. The mixture was kept at 100 °C for 20 hours and then evaporated under reduced pressure. The residue was recrystallized from 10 ml of water, giving 510 mg of biologically active 2,2-dimethyl-1,3-propanediamine, compound with [1,1-cyclobutanedicarboxylato(2-)-O',O']platinum.

Example 6

15 Bis(Acetato-O)bis[sulfinylbis(methane)-S]platinum

A 20.75 g portion of potassium tetrachloroplatinate was added to 165 ml of water, stirred for a few minutes and then filtered. To the filtrate was added 10.65 g of dimethyl sulfoxide. The suspension was allowed to stand for 14 hours, then the crystals were collected, washed with water, ethanol and ether and dried, giving 18.57 g of sulfinylbismethane, compound with platinum chloride.

A suspension of 1.27 g of sulfinylbismethane, compound with platinum chloride, 1.0 g of silver acetate and 70 ml of water was stirred in the dark overnight, then filtered and the filtrate evaporated to dryness. The residue was slurried in methanol, diluted with ether and the solid collected and dried, giving 1.2 g of bis-(acetato-O)-bis[sulfinylbis(methane)-S]platinum.

Example 7

[Propanedioato(2-)-O',O³]bis[sulfinylbis(methane)-S]platinum

A suspension of 1.27 g of sulfinylbismethane, compound with platinum chloride, 953 mg of the disilver salt of malonic acid and 70 ml of water was stirred in the dark overnight, then filtered and the filtrate evaporated to dryness. The residue was slurried in methanol, diluted with ether and the solid collected and dried, giving 1.15 g of [propanedioato(2-)-O',O³]bis[sulfinylbis(methane)-S]-platinum.

Example 8

trans-(-)-[1,1-Cyclobutanedicarboxylato(2-)-O',O']-(1,2-cyclohexanediamine-N,N')[sulfinylbis(methane)-S]platinum

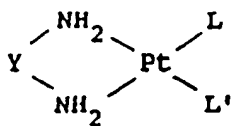
To a solution of 1.24 g of [1,1-cyclobutanedicarboxylato(2-)-O',O']bis[sulfinylbis(methane)-S]platinum in 40 ml of water at 40 °C was added 285 mg of trans-(-)-1,2-cyclohexanediamine. The mixture was heated at 40 °C for 1 hour, then evaporated at 40 °C under reduced pressure. The residue was triturated with ethanol and ether, giving 1.15 g of trans-(-)-[1,1-cyclobutanedicarboxylato(2-)-O',O']-(1,2-cyclohexanediamine-N,N')-[sulfinylbis(methane)-S]-platinum.

A 200 mg portion of the above compound in 5 ml of water was heated at 100 °C for 6 hours, then cooled and the solid collected and dried, giving 130 mg of biologically active trans-(-)-1,2-cyclohexanediamine, compound with [1,1-cyclobutanedicarboxylato(2-)-O',O']platinum.

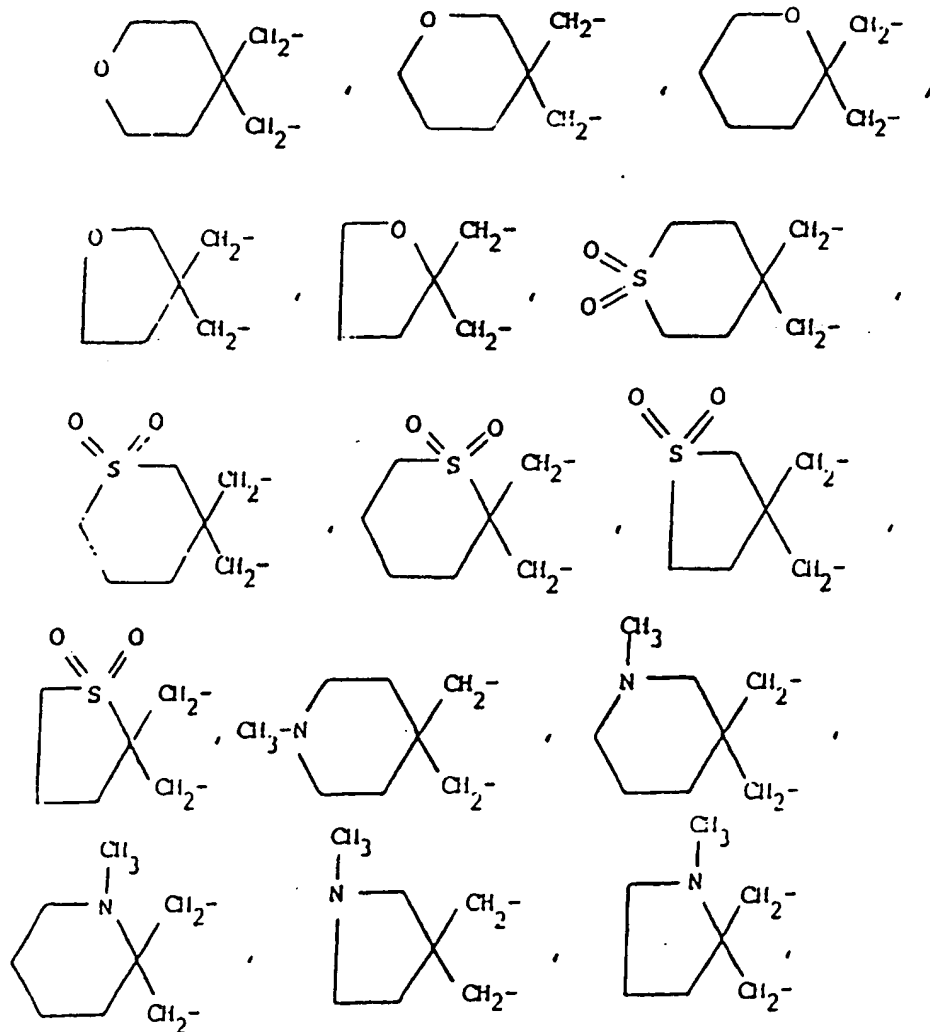
50 Claims

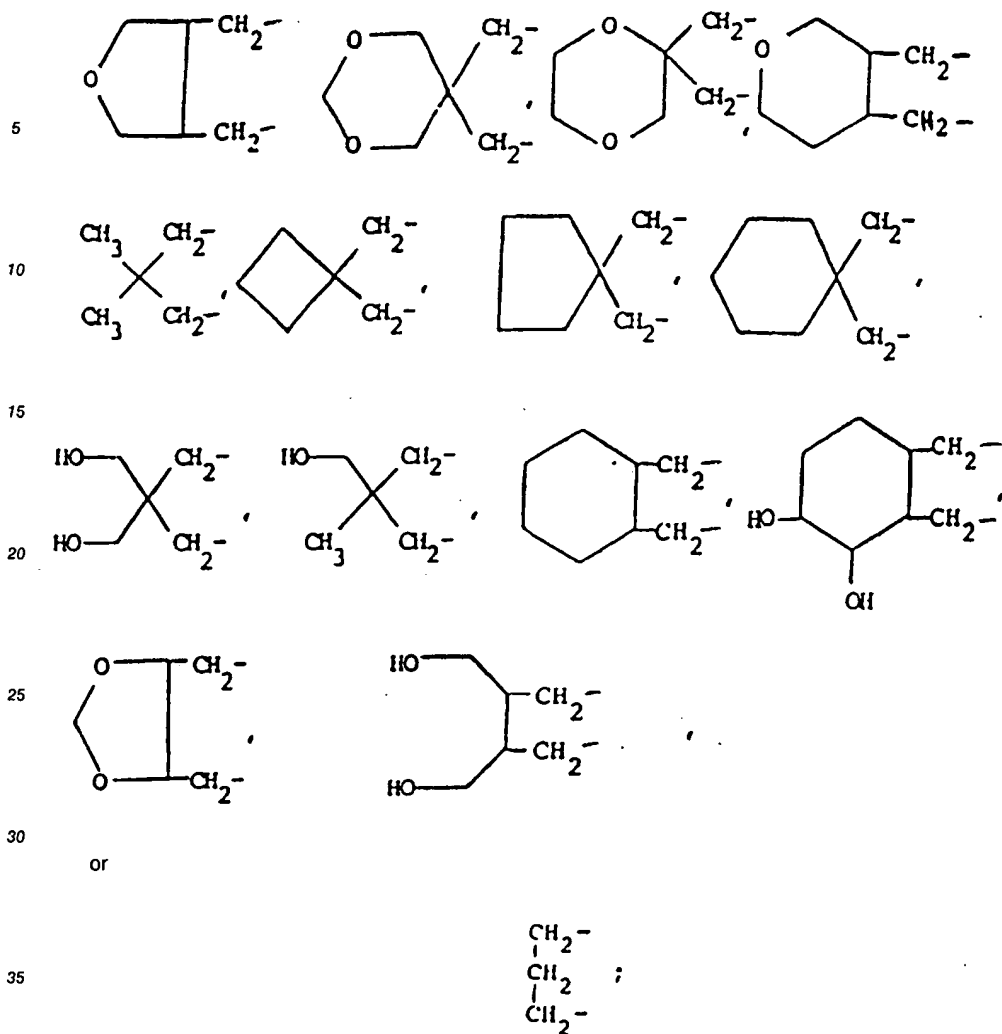
Claims for the following Contracting States : AT, BE, CH, DE, FR, GB, IT, LI, NL, SE

1. A process for producing a compound of the formula:



wherein Y is



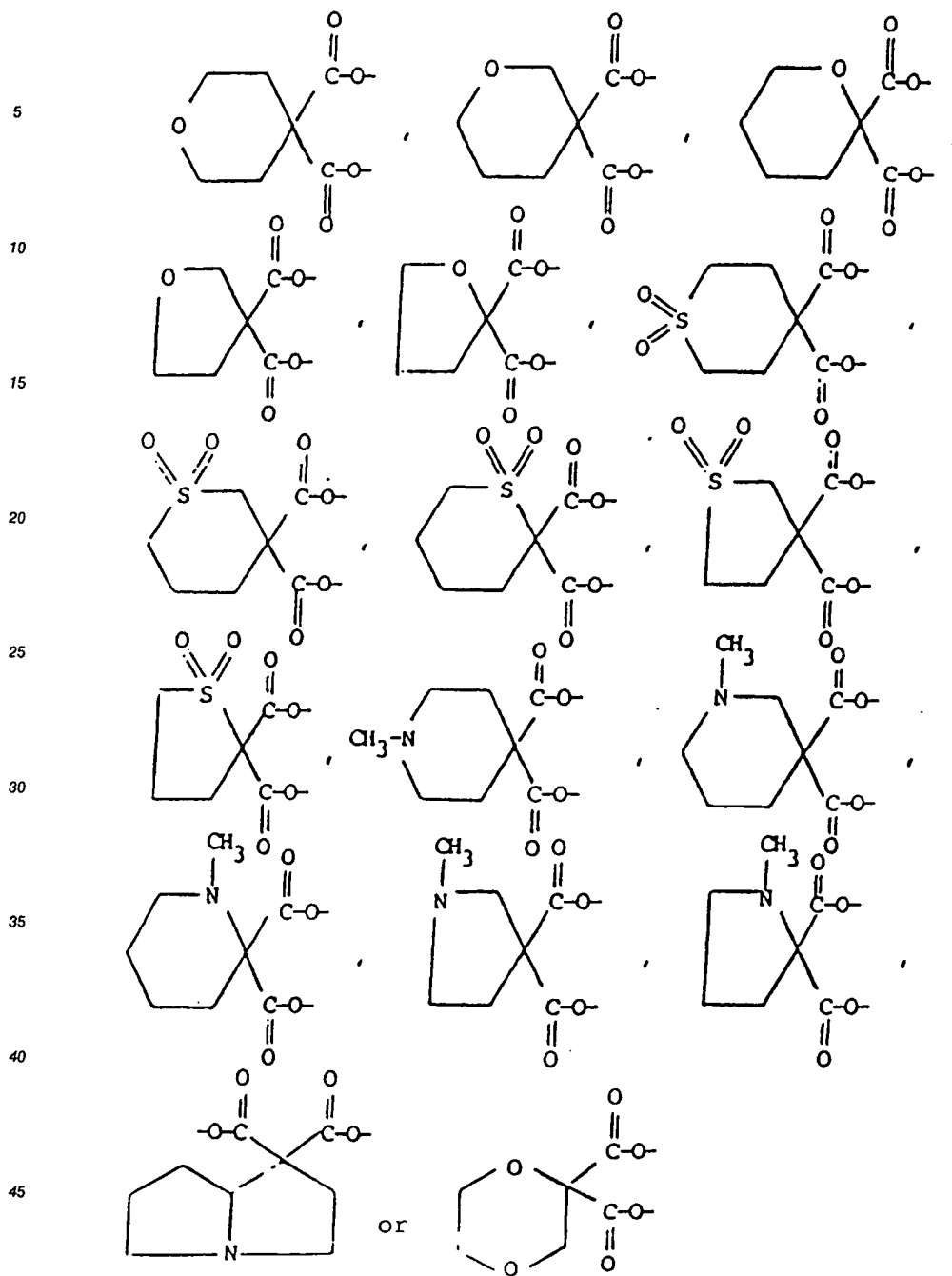


40 and L and L' are monobasic carboxylates consisting of acetate, hydroxyacetate and propionate, or L and L' taken together are a dibasic carboxylate consisting of

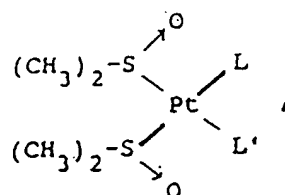


50 where R₁ and R₂ are hydrogen or lower alkyl-(C₁-C₅), or R₁ and R₂ taken together is (CH₂)_n, where n is 2 to 5, or

55



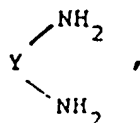
5



10

where L and L' are as described above, which is then reacted with an amine of the formula

15

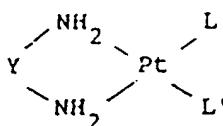


where Y is as described above, in a hot aqueous solution.

20

2. A process for producing a compound of the formula:

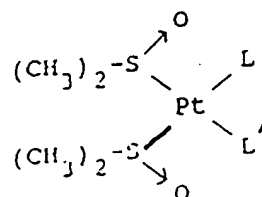
25



30

wherein Y, L and L' are as defined in claim 1, which comprises reacting a carboxylic acid-bis[sulfinylbis [methane]-S]platinum compound of the formula

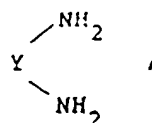
35



40

where L and L' are as defined in Claim 1, in warm aqueous solution with an amine of the formula

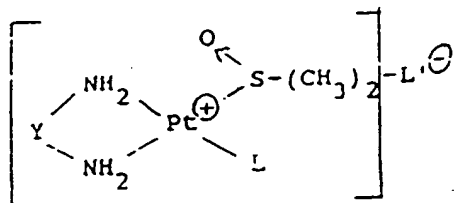
45



50

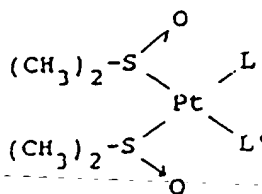
where Y is as defined in Claim 1, giving a compound of the formula:

55



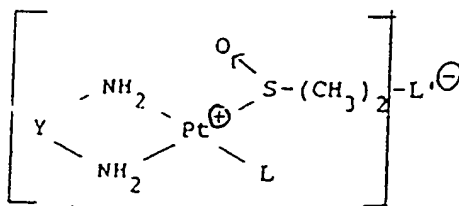
which is further reacted in a hot aqueous solution.

3. A compound of the formula:



wherein L and L' are as defined in Claim 1.

4. The compound according to claim 3, [1,1-cyclobutanedicarboxylato(2-)-O,O']bis[sulfinylbis(methane)-S]-platinum.
5. The compound according to Claim 3, bis(aceto-O)bis[sulfinylbis(methane)-S]platinum.
6. The compound according to Claim 3 [propanedioato(2-)-O',O³]bis[sulfinylbis(methane)-S] platinum.
7. A compound of the formula :

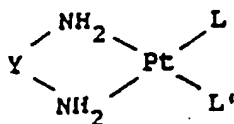


wherein Y, L and L' are as defined in Claim 1.

8. The compound according to Claim 7, trans(-)-[1,1-cyclobutanedicarboxylato(2-)-O,O'](1,2-cyclohexanediamine-N,N')[sulfinylbis(methane)-S] platinum.

50 Claims for the following Contracting States : ES, GR

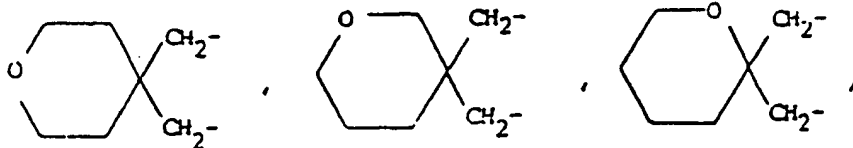
1. A process for producing a compound of the formula:



5

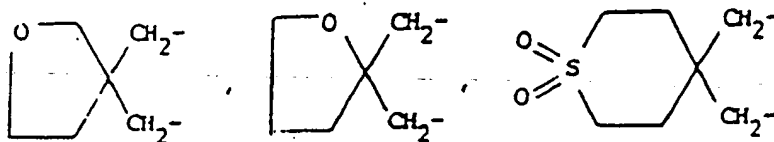
wherein Y is

10

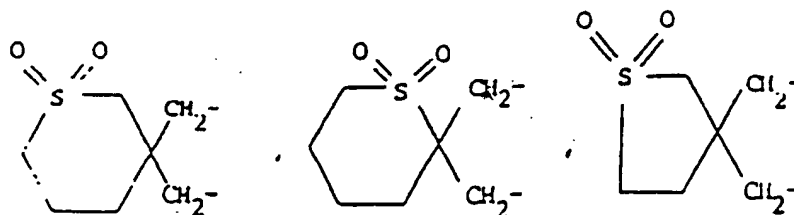


15

20

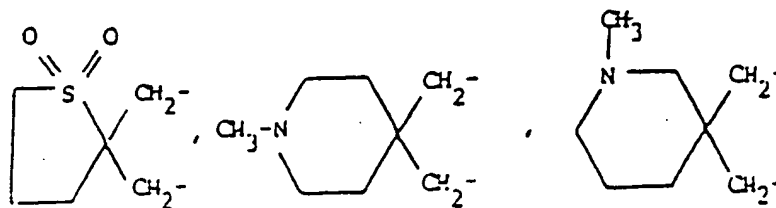


25

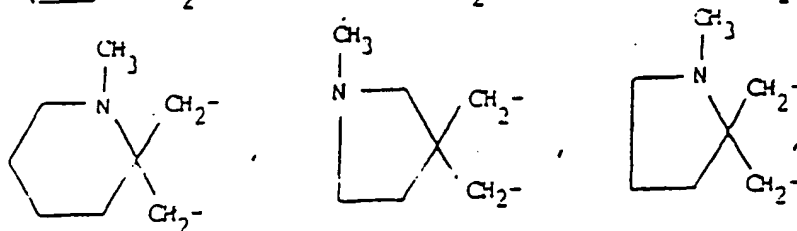


30

35



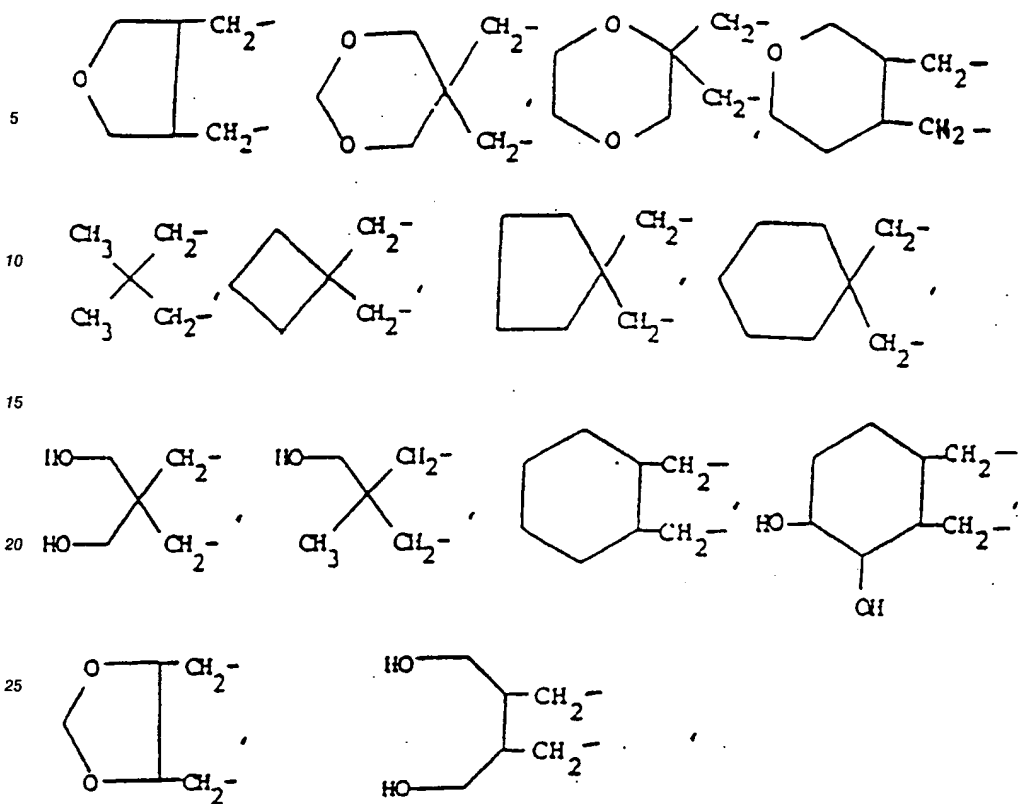
40



45

50

55



or

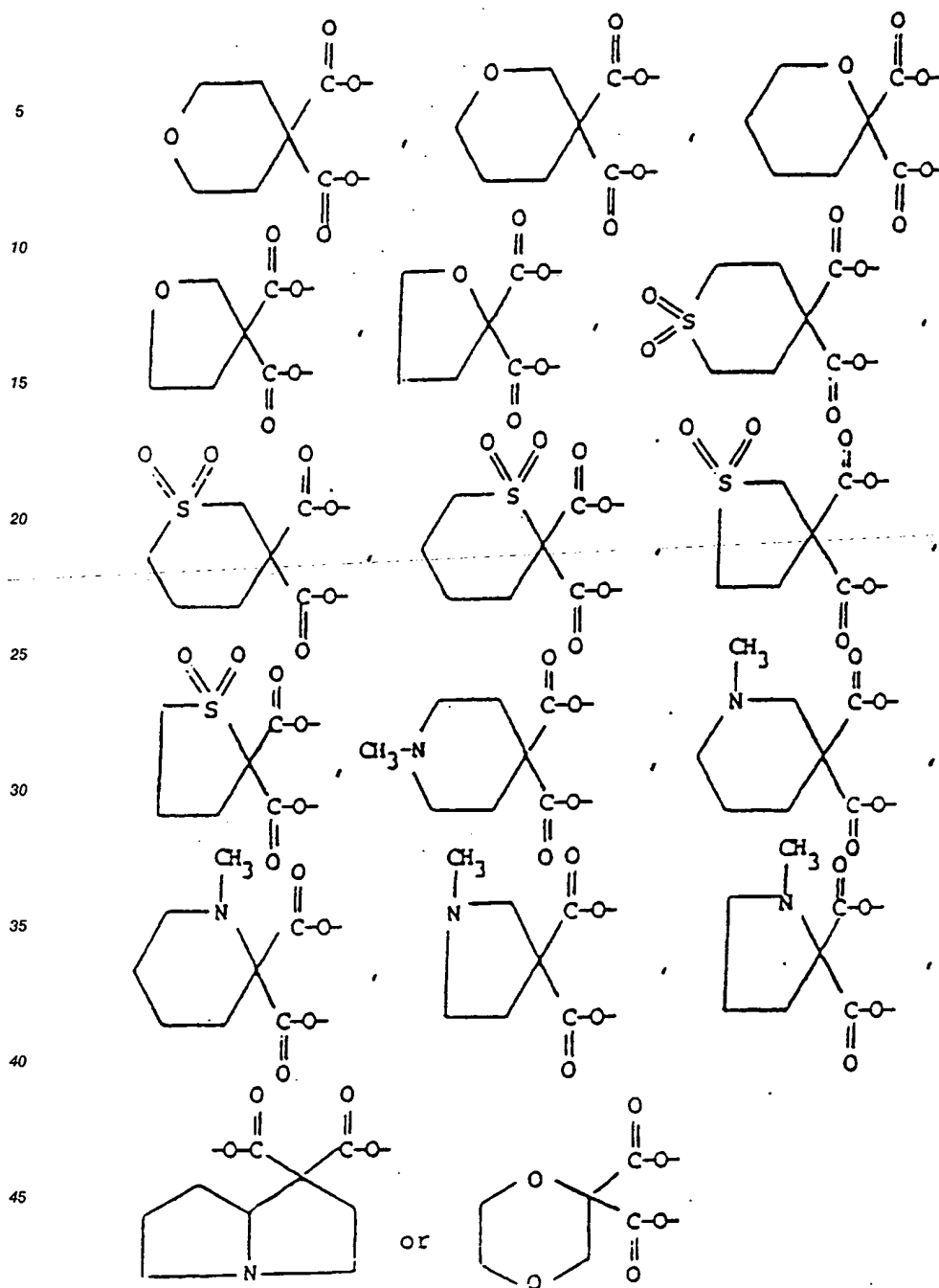


40 and L and L' are monobasic carboxylates consisting of acetate, hydroxyacetate and propionate, or L and L' taken together are a dibasic carboxylate consisting of

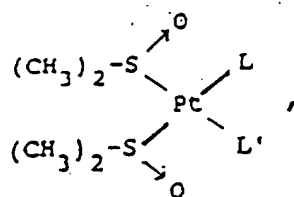


50 where R₁ and R₂ are hydrogen or lower alkyl-(C₁-C₅), or R₁ and R₂ taken together is (CH₂)_n, where n is 2 to 5, or

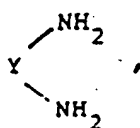
55



which comprises reacting sulfinylbismethane, compound with platinum chloride with mono- or dicarboxylic acid silver salt in aqueous solution, protected from the light, giving a carboxylic acid-bis[sulfinylbis-[methane]-S]platinum compound of the formula where L and

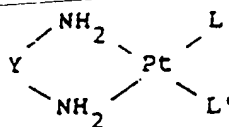


L' are as described above, which is then reacted with an amine of the formula

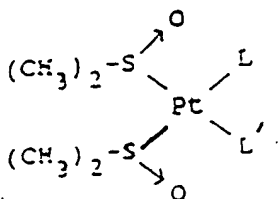


where Y is as described above, in a hot aqueous solution.

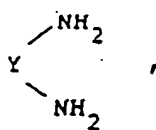
2. A process for producing a compound of the formula:



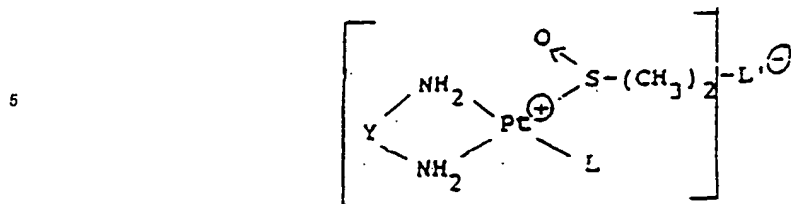
wherein Y, L and L' are as defined in Claim 1, which comprises reacting a carboxylic acid-bis(sulfinylbis [methane]-S)platinum compound of the formula,



where L and L' are as defined in Claim 1, in warm aqueous solution with an amine of the formula



where Y is as defined in Claim 1, giving a compound of the formula:



10

which is further reacted in a hot aqueous solution.

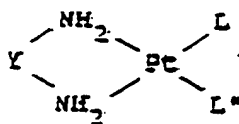
Patentansprüche

Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, DE, FR, GB, IT, LI, NL, SE

15

1. Verfahren zur Herstellung einer Verbindung der Formel

20



25

wobei Y für eine Gruppe der folgenden Formeln steht:

30

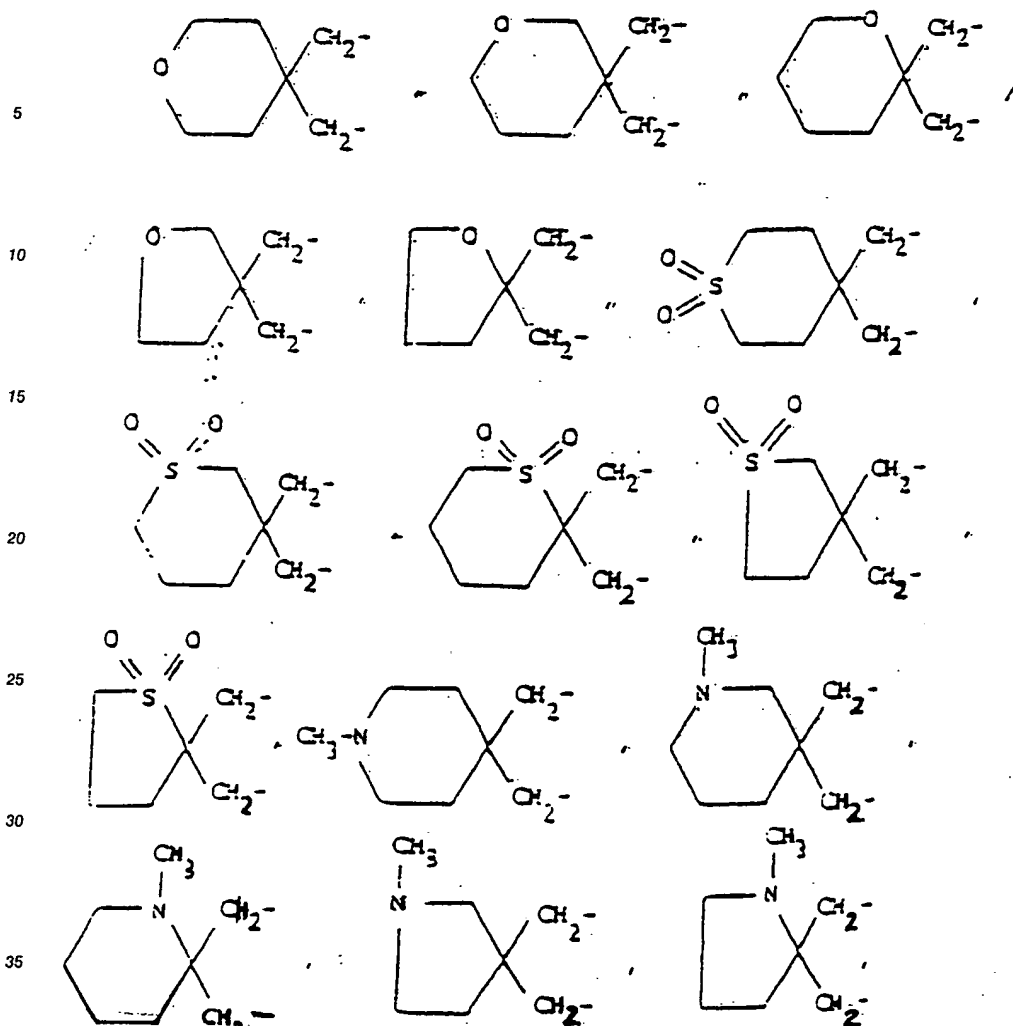
35

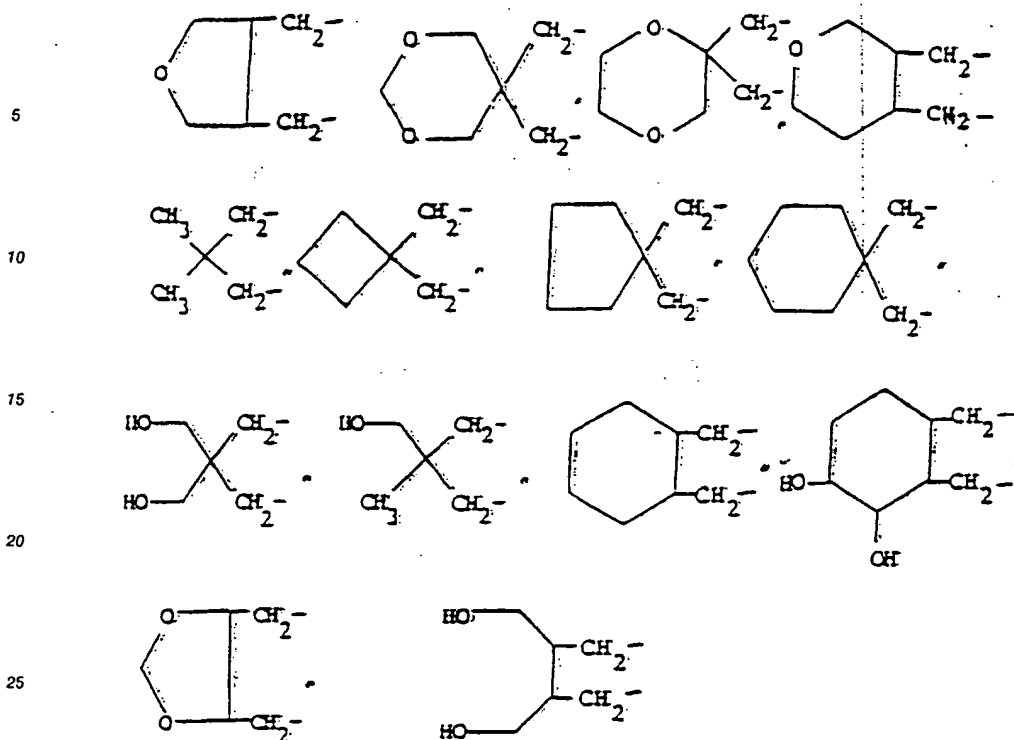
40

45

50

55





30 oder



und wobei L und L' einbasische Carboxylate, bestehend aus Acetat, Hydroxyacetat und Propionat sind,
oder wobei L und L' ein zweibasches Carboxylat bilden, bestehend aus

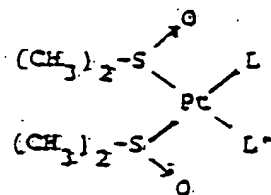


wobei R₁ und R₂ Wasserstoff oder Nieder-alkyl-(C₁-C₅) sind, oder wobei R₁ oder R₂ zusammen (CH₂)_n,
bedeuten, wobei n für 2 bis 5 steht oder

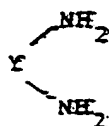
55



55

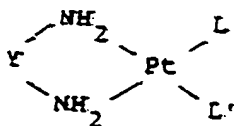


in der L und L' die oben angegebene Bedeutung, haben, welche sodann umgesetzt wird mit einem Amin der Formel

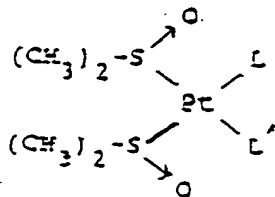


wobei Y die oben angegebene Bedeutung hat, und zwar in einer heißen wässrigen Lösung.

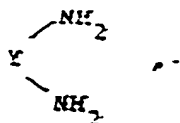
2. Verfahren zur Herstellung einer Verbindung der Formel



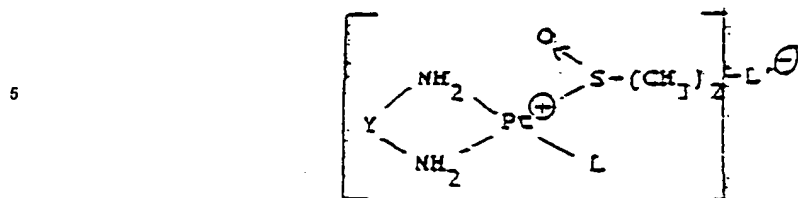
wobei Y, L und L' die in Anspruch 1 angegebene Bedeutung haben, wobei man eine Carbonsäure-bis-[sulfanylbis(methan)-S]platin-Verbindung der Formel



in der L und L' die in Anspruch 1 angegebene Bedeutung haben, in warmer, wässriger Lösung umgesetzt mit einem Amin der Formel



wobei Y die in Anspruch 1 angegebene Bedeutung hat, unter Bildung einer Verbindung der Formel



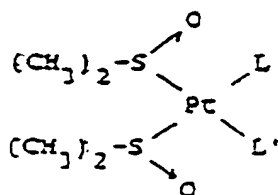
10

welche sodann in heißer wässriger Lösung umgesetzt wird.

3. Verbindung der Formel

15

20



wobei L und L' die in Anspruch 1 angegebene Bedeutung haben.

25

4. Verbindung nach Anspruch 3, [1,1-Cyclobutandicarboxylato(2-)-O,O']bis[sulfinylbis[methan]-S]platin.

5. Verbindung nach Anspruch 3, Bis-(aceto-O)-bis[sulfinylbis[methan]-S]platin.

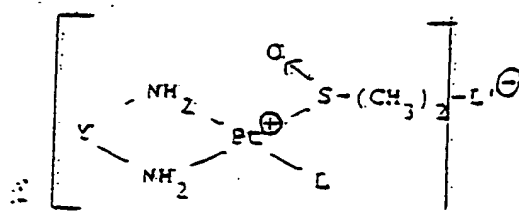
30

6. Verbindung nach Anspruch 3, [Propandioato(2-)-O,O']bis[sulfinylbis[methan]-S]platin.

7. Verbindung der Formel

35

40



wobei Y, L und L' die in Anspruch 1 angegebene Bedeutung haben.

45

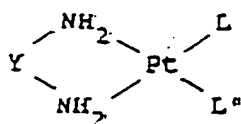
8. Verbindung nach Anspruch 7, trans-(1,1-Cyclobutandicarboxylato(2-)-O,O')bis[1,2-cyclohexandiamin-N,N']bis[sulfinylbis[methan]-S]platin.

Patentansprüche für folgende Vertragsstaaten : ES, GR

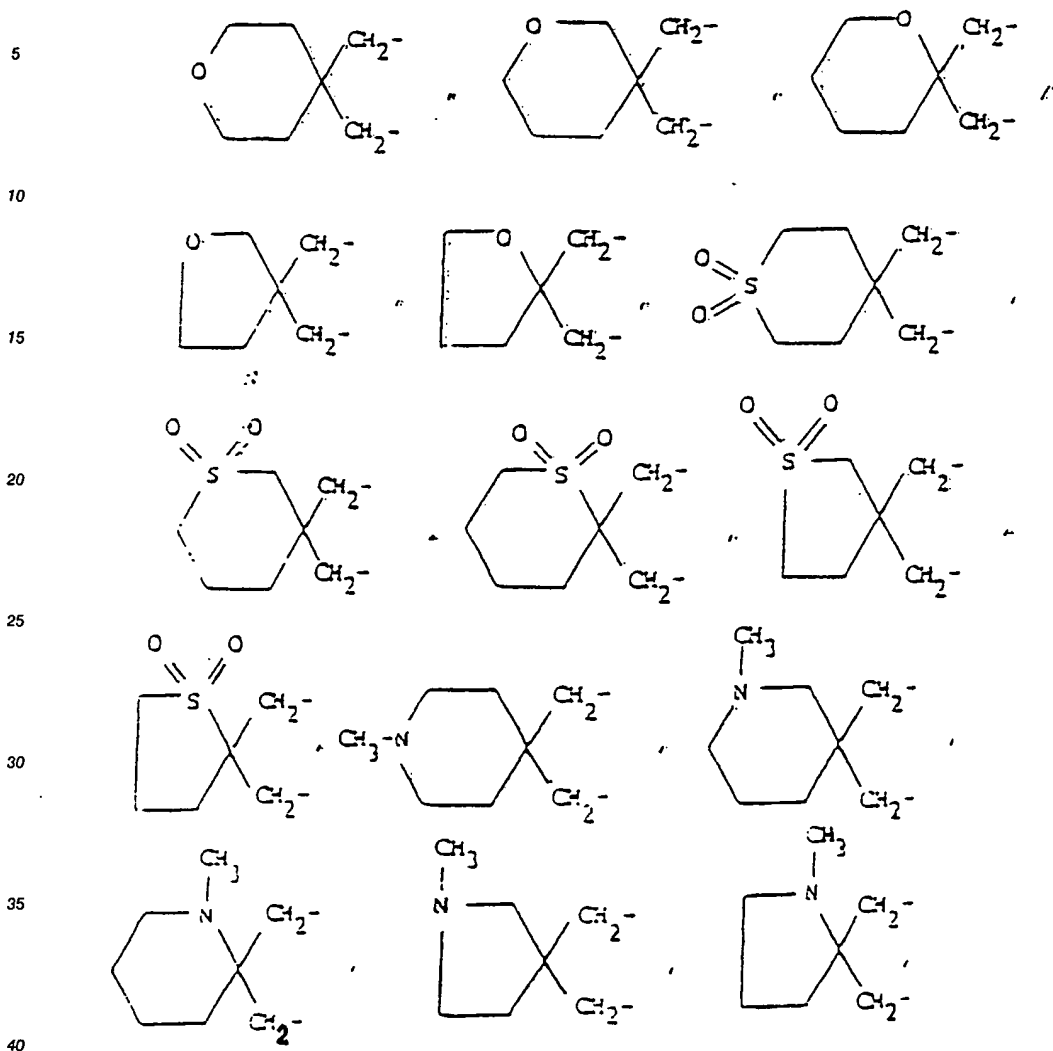
50

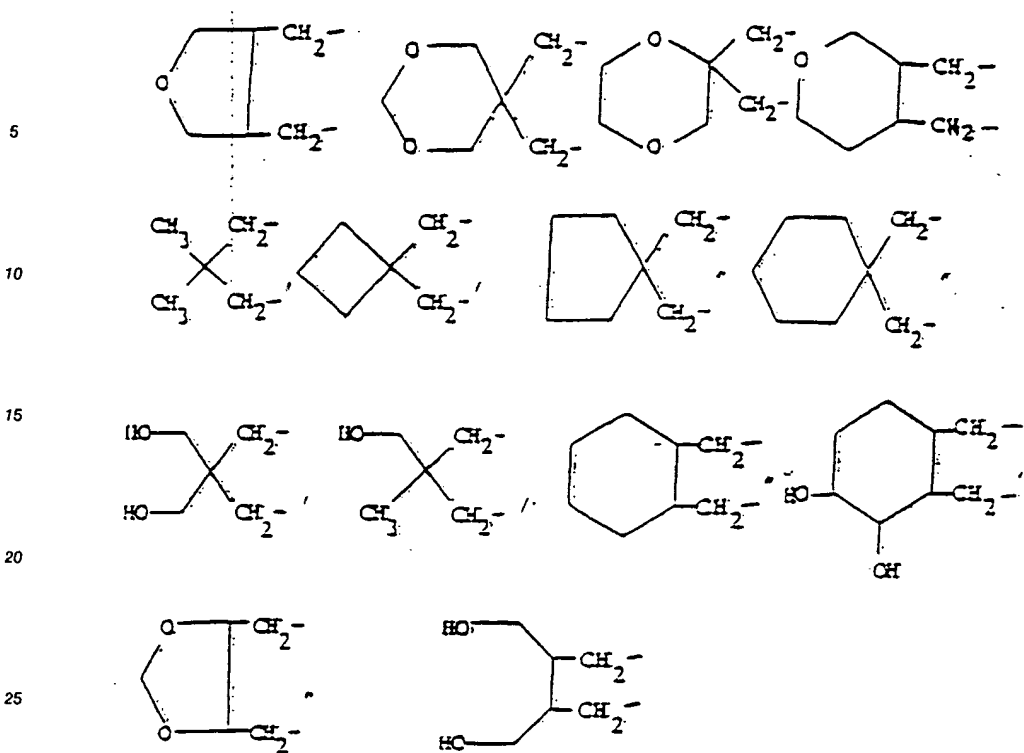
1. Verfahren zur Herstellung einer Verbindung der Formel

55



wobei Y für eine Gruppe der folgenden Formeln steht:





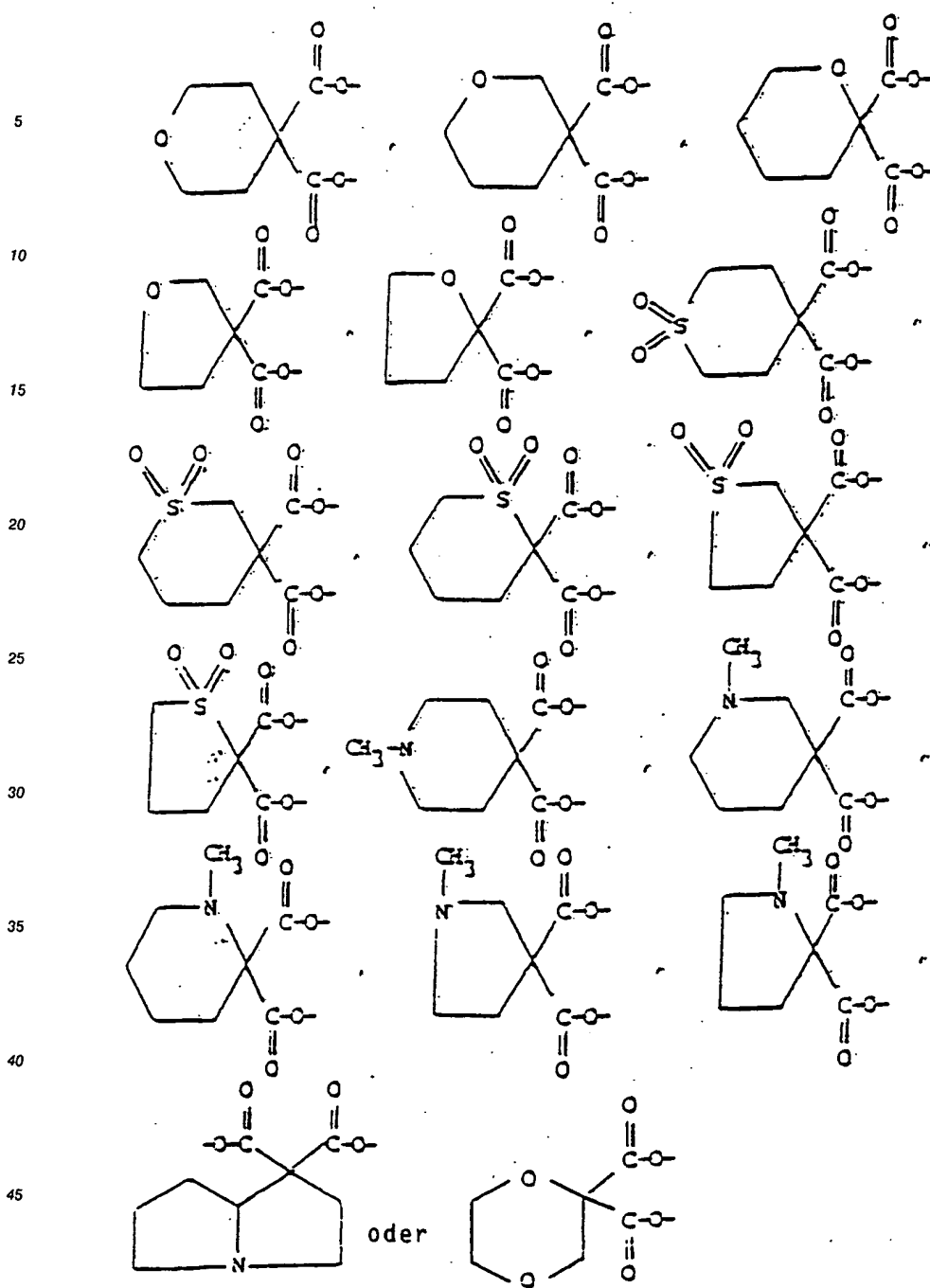
oder



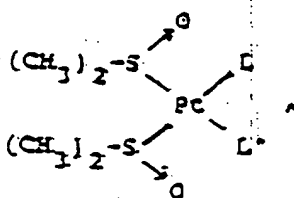
und wobei L und L' einbasische Carboxylate, bestehend aus Acetat, Hydroxyacetat und Propionat sind,
oder wobei L und L' ein zweibasisches Carboxylat bilden bestehend aus



wobei R₁ und R₂ Wasserstoff oder Nieder-alkyl-(C₁-C₅) sind, oder wobei R₁ oder R₂ zusammen (CH₂)_n,
bedeuten, wobei n für 2 bis 5 steht, oder

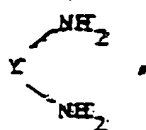


wobei man eine Verbindung von Sulfinylbismethan mit Platinchlorid mit Mono- oder Dicarbonsäuresilbersalz in wässriger Lösung unter Ausschluß von Licht umsetzt unter Bildung einer Carbonsäure-bis-[sulfinylbis(methan)-S]platin-Verbindung der Formel



5

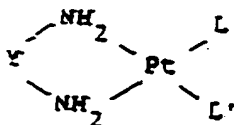
10 in der L und L' die oben angegebene Bedeutung haben, welche sodann umgesetzt wird mit einem Amin der Formel



15

20 wobei Y die oben angegebene Bedeutung hat und zwar in einer heißen wässrigen Lösung.

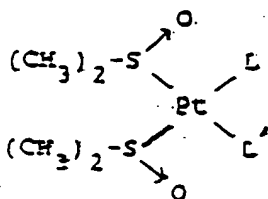
2. Verfahren zur Herstellung einer Verbindung der Formel



25

30

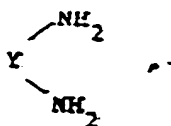
wobei Y, L und L' die in Anspruch 1 angegebene Bedeutung haben, wobei man eine Carbonsäure-bis-[sulfinylbis(methan)-S]platin-Verbindung der Formel



35

40

45 in der L und L' die in Anspruch 1 angegebene Bedeutung haben, in warmer, wässriger Lösung umgesetzt mit einem Amin der Formel

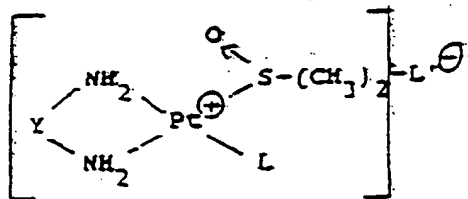


50

wobei Y die in Anspruch 1 angegebene Bedeutung hat, unter Bildung einer Verbindung der Formel

55

5



10

welche sodann in heißer wässriger Lösung umgesetzt wird.

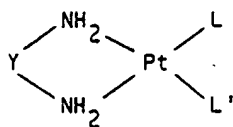
Revendications

Revendications pour les Etats contractants suivants : AT, BE, CH, DE, FR, GB, IT, LI, NL, SE

15

1. Un procédé pour produire un composé de formule :

20



25

dans laquelle Y est

30

35

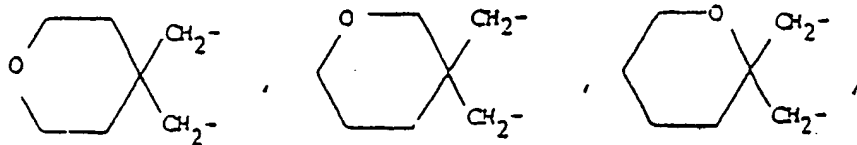
40

45

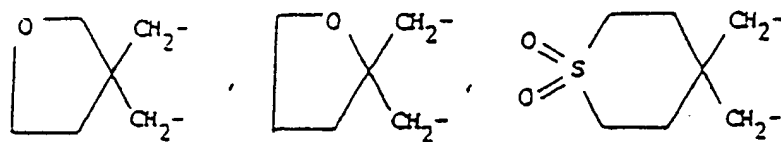
50

55

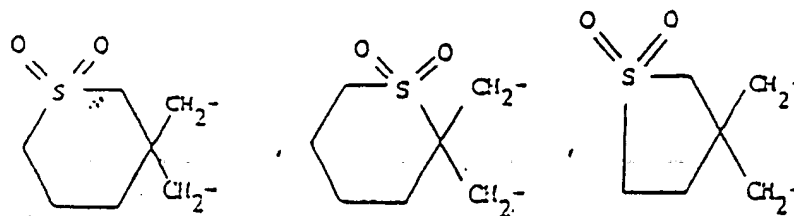
5



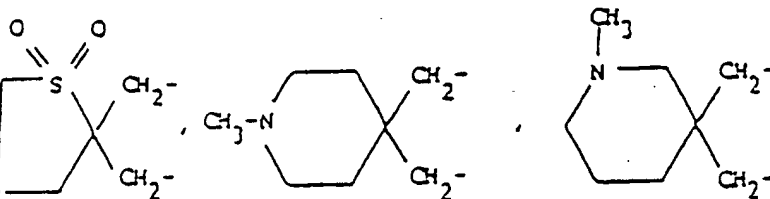
10



15

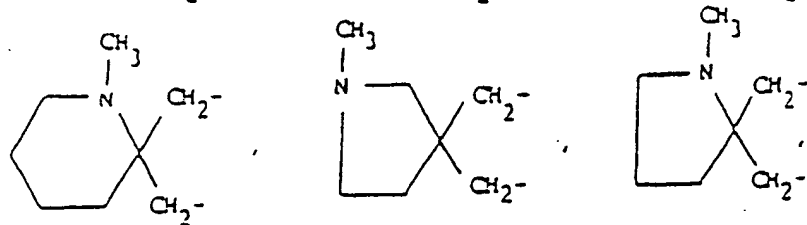


20



25

30



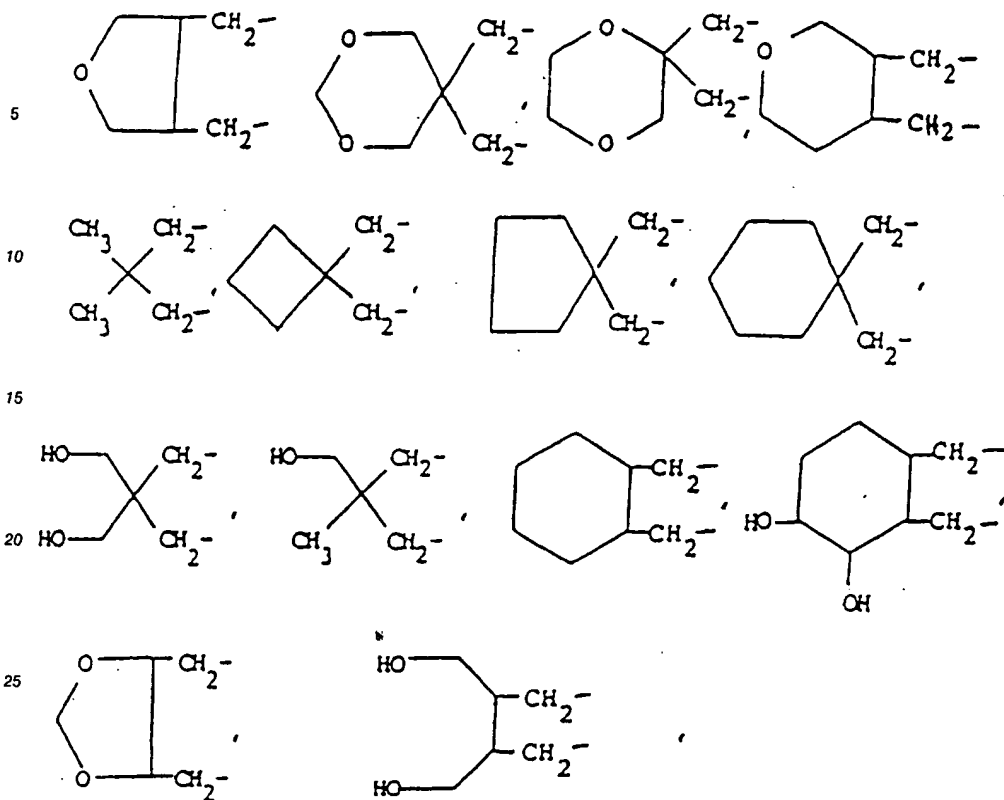
35

40

45

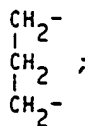
50

55



ou

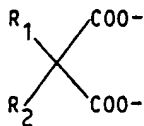
35



40

et L et L' sont des restes monocarboxylates choisis parmi acétate, hydroxyacétate et propionate, ou bien L et L' pris ensemble forment un reste dicarboxylate

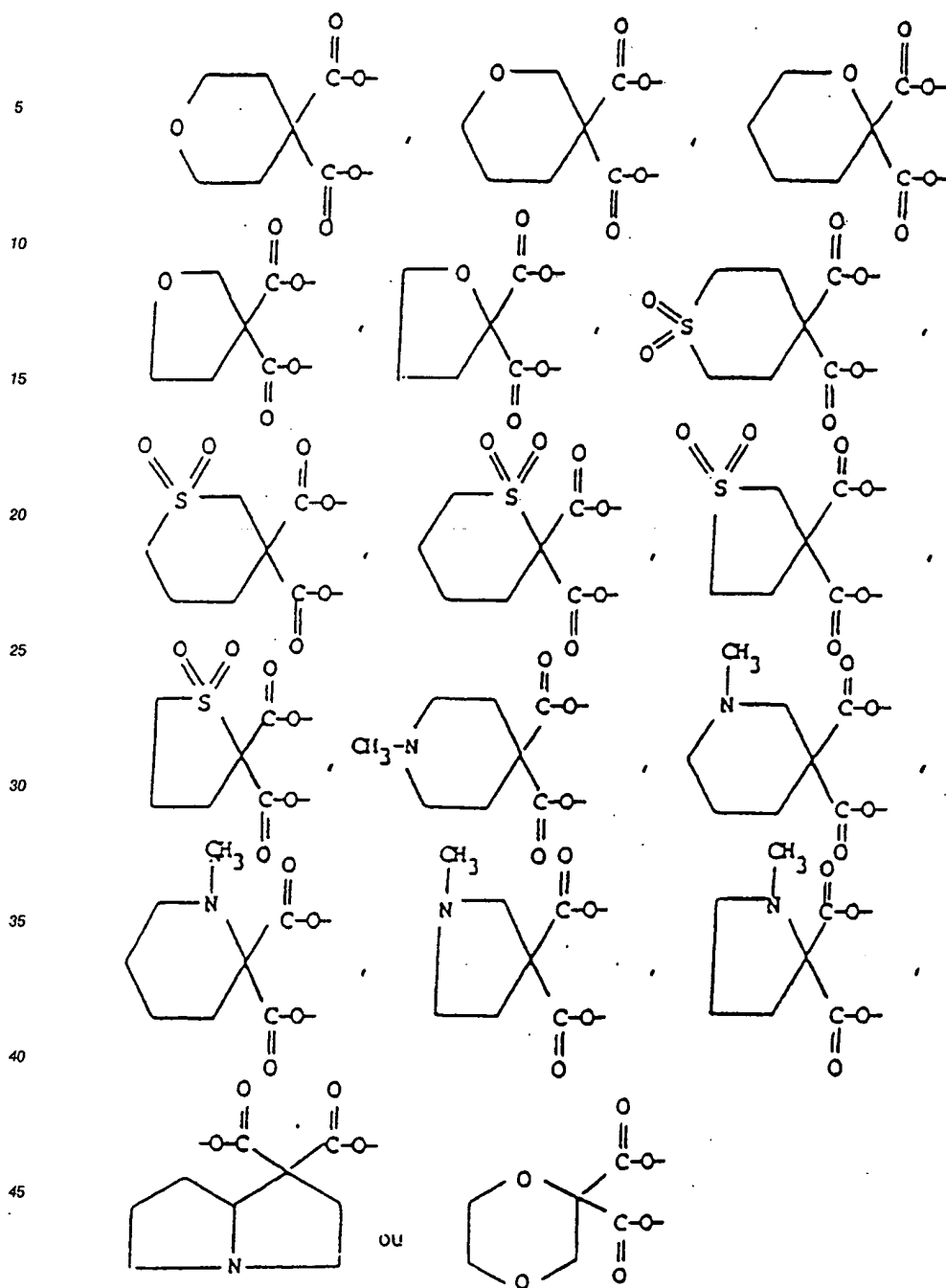
45



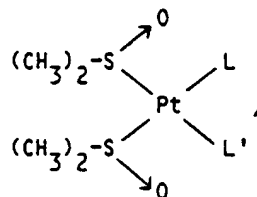
50

où R₁ et R₂ sont chacun l'hydrogène ou un groupe alkyle inférieur en C₁-C₅, ou bien R₁ et R₂ pris ensemble forment un groupe (CH₂)_n, dans lequel n est un nombre de 2 à 5, ou bien

55

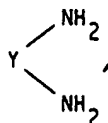


caractérisé en ce qu'il consiste à faire réagir un composé de sulfinylbisméthane-chlorure de platine avec un sel d'argent d'acide mono- ou dicarboxylique en solution aqueuse, à l'abri de la lumière, pour donner un composé acide carboxylique-bis[sulfinylbis[méthane]-S]platine de formule :



5

10 dans laquelle L et L' sont comme décrit ci-dessus, que l'on fait ensuite réagir avec une amine de formule

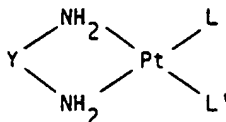


15

dans laquelle Y est comme décrit ci-dessus, dans une solution aqueuse chaude.

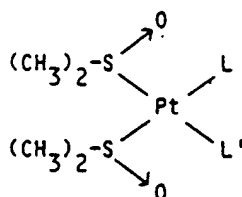
20

2. Un procédé pour produire un composé de formule :



25

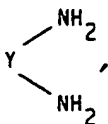
30 dans laquelle Y, L et L' sont définis comme à la revendication 1, caractérisé en ce qu'il consiste à faire réagir un composé acide carboxylique-bis[sulfinylbis[méthane]-S]platine de formule :



35

40

dans laquelle L et L' sont définis comme à la revendication 1, en solution aqueuse chaude avec une amine de formule

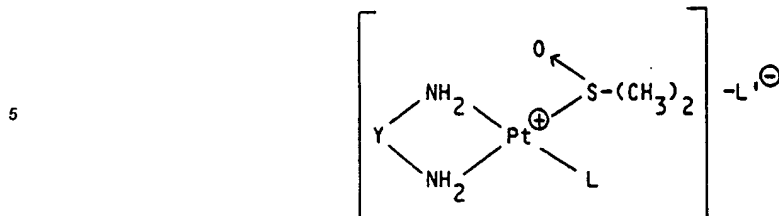


45

50

dans laquelle Y est tel que défini à la revendication 1, pour donner un composé de formule :

55



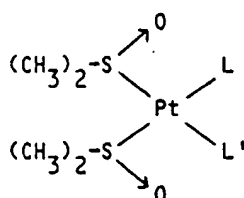
10

que l'on fait encore réagir dans une solution aqueuse chaude.

3. Un composé, caractérisé en ce qu'il répond à la formule :

15

20



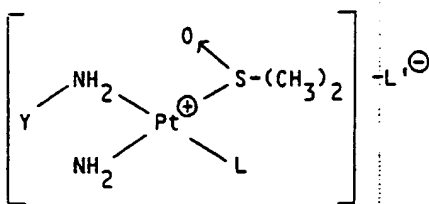
25

dans laquelle L et L' sont tels que définis à la revendication 1.

4. Le composé selon la revendication 3, caractérisé en ce qu'il consiste en le [1,1-cyclobutanedicarboxylato(2-)-O,O']bis[sulfinylbis[méthane]-S]platine.
- 30 5. Le composé selon la revendication 3, caractérisé en ce qu'il consiste en le bis(acéto-O)bis[sulfinylbis[méthane]-S]platine.
6. Le composé selon la revendication 3, caractérisé en ce qu'il consiste en le [propanedioato(2-)-O',O³]-bis[sulfinylbis[méthane]-S]platine.
- 35 7. Un composé, caractérisé en ce qu'il répond à la formule :

40

45

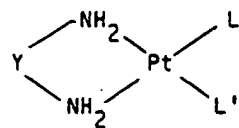


dans laquelle Y, L et L' sont tels que définis à la revendication 1.

- 50 8. Le composé selon la revendication 7, caractérisé en ce qu'il consiste en le trans-(-)-[1,1-cyclobutanedicarboxylato(2-)-O,O'][(1,2-cyclohexanediamine-N,N')][sulfinylbis[méthane]-S]platine.

Revendications pour les Etats contractants suivants : ES, GR

- 55 1. Un procédé pour produire un composé de formule :



5

dans laquelle Y est

10

15

20

25

30

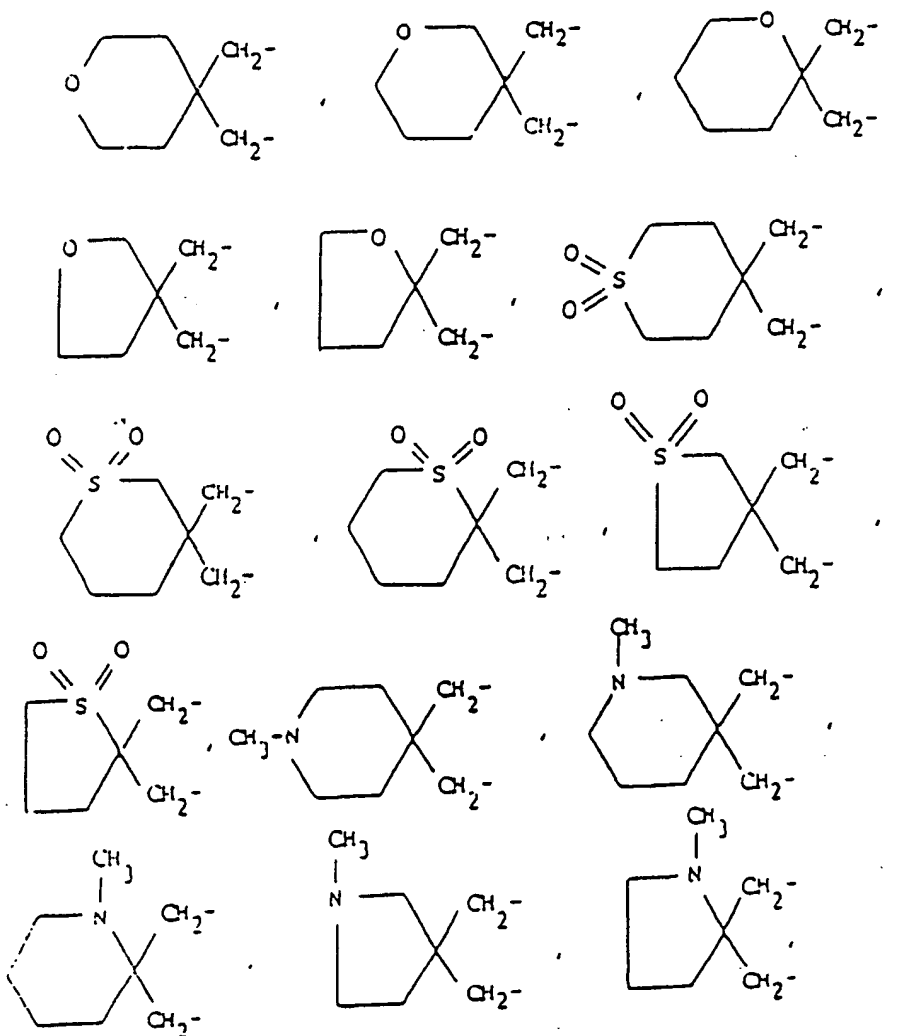
35

40

45

50

55

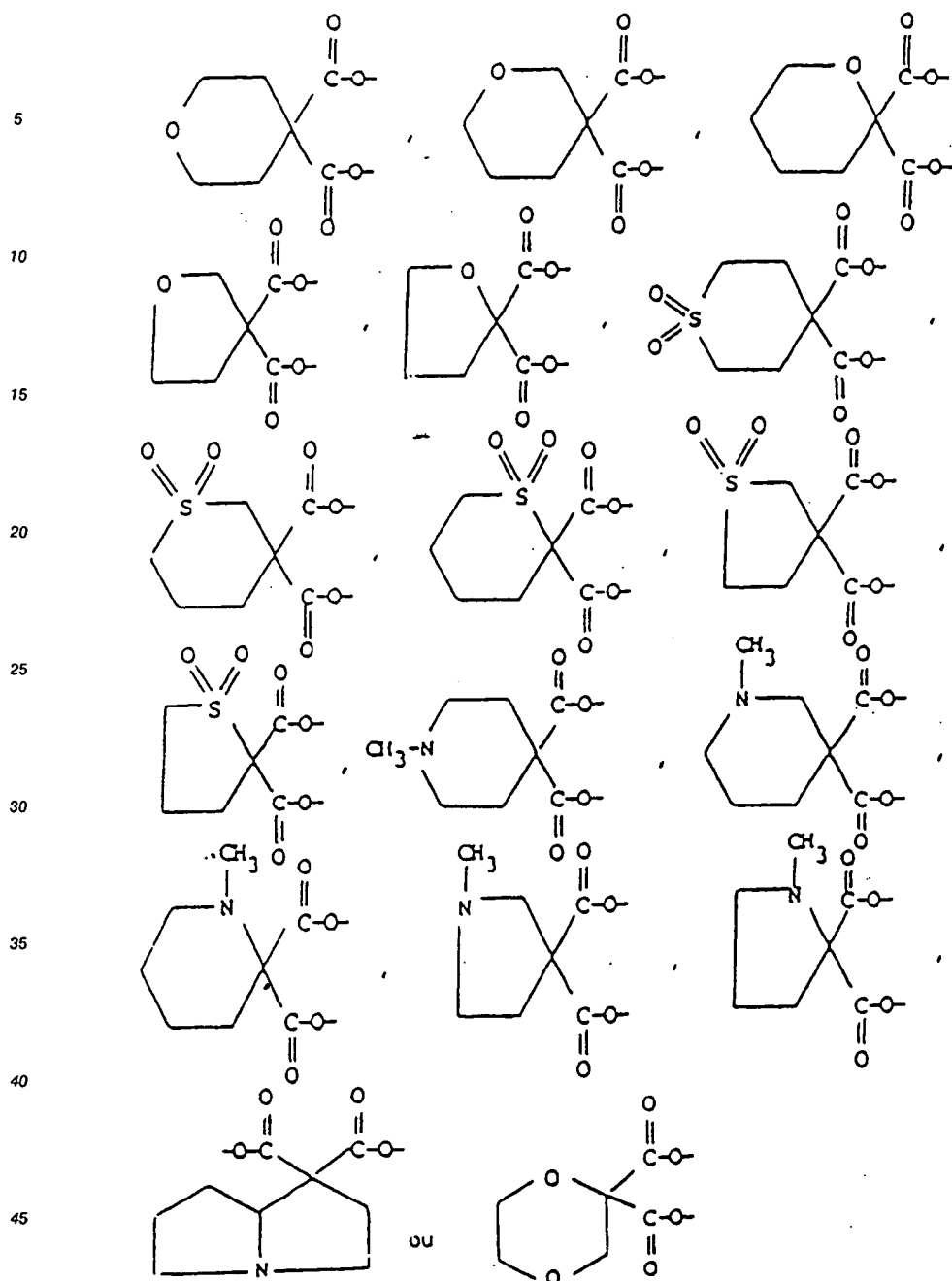




40

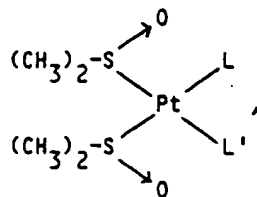


50



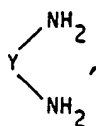
50 caractérisé en ce qu'il,consiste à faire réagir un composé de sulfinylbisméthane-chlorure de platine avec un sel d'argent d'acide mono- ou dicarboxylique en solution aqueuse, à l'abri de la lumière, pour donner un composé acide carboxylique-bis[sulfinylbis[méthane]-S]platine de formule :

55



5

10 dans laquelle L et L' sont comme décrit ci-dessus, que l'on fait ensuite réagir avec une amine de formule

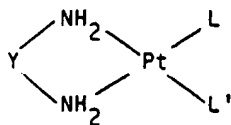


15

dans laquelle Y est comme décrit ci-dessus, dans une solution aqueuse chaude.

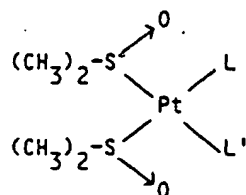
20

2. Un procédé pour produire un composé de formule :



25

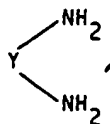
30 dans laquelle Y, L et L' sont définis comme à la revendication 1, caractérisé en ce qu'il consiste à faire réagir un composé acide carboxy[ique-bis[sulfinylbis[méthane]-S]platine de formule :



35

40

dans laquelle L et L' sont définis comme à la revendication 1, en solution aqueuse chaude avec une amine de formule

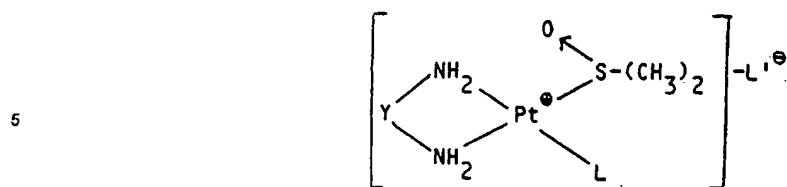


45

50

dans laquelle Y est tel que défini à la revendication 1, pour donner un composé de formule :

55



10 que l'on fait encore réagir dans une solution aqueuse chaude.

15

20

25

30

35

40

45

50

55

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.